



**University of
Zurich**^{UZH}

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2008

Contemporary management of octogenarians hospitalized for heart failure in Europe: Euro Heart Failure Survey II

Komajda, M ; Hanon, O ; Hochadel, M ; Lopez-Sendon, J L ; Follath, F ; Ponikowski, P ; Harjola, V P ; Drexler, H ; Dickstein, K ; Tavazzi, L ; Nieminen, M

Abstract: Aims International guidelines are frequently not implemented in the elderly population with heart failure (HF). This study determined the management of octogenarians with HF enrolled in Euro Heart Failure Survey II (EHFS II) (2004-05). **Methods and results** We compared the clinical profile, 12 month outcomes, and management modalities between 741 octogenarians (median age 83.7 years) and 2836 younger patients (median age 68.4 years) hospitalized for acute/decompensated HF. Management modalities were also compared with those observed in EHFS I (2000-01). Female gender, new onset HF (de novo), hypertension, atrial fibrillation, co-morbidities, disabilities, and low quality of life were more common in the elderly (all $P < 0.001$). Mortality rates during hospital stay and during 12 months after discharge were increased in octogenarians (10.7 vs. 5.6% and 28.4 vs. 18.5%, $P < 0.001$). Underuse and underdosage of medications recommended for HF were observed in the elderly. However, a significant improvement was observed when compared with EHFS I both in the overall HF octogenarian population and in the subgroup with ejection fraction $\geq 45\%$ for prescription rates of ACE-I/ARBs, beta-blockers, and aldosterone antagonists at discharge (82 vs. 71%; 56 vs. 29%; 54 vs. 18.5%, respectively, all $P < 0.01$), as well as for recommended combinations and dosage. Prescription rates remained stable for 12 months after discharge in survivors. **Conclusion** Our study confirms that the contemporary management of very elderly patients with HF remains suboptimal but that the situation is improving

DOI: <https://doi.org/10.1093/eurheartj/ehn539>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-155555>

Journal Article

Published Version

Originally published at:

Komajda, M; Hanon, O; Hochadel, M; Lopez-Sendon, J L; Follath, F; Ponikowski, P; Harjola, V P; Drexler, H; Dickstein, K; Tavazzi, L; Nieminen, M (2008). Contemporary management of octogenarians hospitalized for heart failure in Europe: Euro Heart Failure Survey II. *European Heart Journal*, 30(4):478-486.

DOI: <https://doi.org/10.1093/eurheartj/ehn539>

Contemporary management of octogenarians hospitalized for heart failure in Europe: Euro Heart Failure Survey II

Michel Komajda^{1*}, Olivier Hanon², Matthias Hochadel³, Jose Luis Lopez-Sendon⁴, Ferenc Follath⁵, Piotr Ponikowski⁶, Veli-Pekka Harjola⁷, Helmut Drexler⁸, Kenneth Dickstein⁹, Luigi Tavazzi^{8,10}, and Markku Nieminen⁷

¹AP-HP, Department of Cardiology, Pitie Salpetriere Hospital, University Pierre et Marie Curie-Paris 6, 47/83, boulevard de l'Hôpital, Paris 75013, France; ²AP-HP, Department of Geriatrics, Broca Hospital, University Paris-Descartes-Paris 5, Paris, France; ³Stiftung Institut für Herzinfarktforschung an der Universität Heidelberg, Ludwigshafen am Rhein, Germany; ⁴Department of Cardiology, University Hospital La Paz, Paseo de la Castellana, 261 Madrid, Spain; ⁵Department of Cardiology, University Hospital, Zurich, Switzerland; ⁶Klinika Kardiologi, Wojskowy Szpital Kliniczny z Poliklinika, Wrocław, Poland; ⁷Department of Medicine, University Hospital, Helsinki, Finland; ⁸Zentrum Innere Medizin Med. Hochschule, Hannover, Germany; ⁹Cardiology Division, Stavanger University Hospital, University of Bergen 4011, Stavanger, Norway; and ¹⁰Department of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Received 27 May 2008; revised 3 November 2008; accepted 6 November 2008; online publish-ahead-of-print 23 December 2008

See page 391 for the editorial comment on this article (doi:10.1093/eurheartj/ehp024)

Aims

International guidelines are frequently not implemented in the elderly population with heart failure (HF). This study determined the management of octogenarians with HF enrolled in Euro Heart Failure Survey II (EHFS II) (2004–05).

Methods and results

We compared the clinical profile, 12 month outcomes, and management modalities between 741 octogenarians (median age 83.7 years) and 2836 younger patients (median age 68.4 years) hospitalized for acute/decompensated HF. Management modalities were also compared with those observed in EHFS I (2000–01). Female gender, new onset HF (*de novo*), hypertension, atrial fibrillation, co-morbidities, disabilities, and low quality of life were more common in the elderly (all $P < 0.001$). Mortality rates during hospital stay and during 12 months after discharge were increased in octogenarians (10.7 vs. 5.6% and 28.4 vs. 18.5%, $P < 0.001$). Underuse and underdosage of medications recommended for HF were observed in the elderly. However, a significant improvement was observed when compared with EHFS I both in the overall HF octogenarian population and in the subgroup with ejection fraction $\leq 45\%$ for prescription rates of ACE-I/ARBs, beta-blockers, and aldosterone antagonists at discharge (82 vs. 71%; 56 vs. 29%; 54 vs. 18.5%, respectively, all $P < 0.01$), as well as for recommended combinations and dosage. Prescription rates remained stable for 12 months after discharge in survivors.

Conclusion

Our study confirms that the contemporary management of very elderly patients with HF remains suboptimal but that the situation is improving.

Keywords

Heart failure • Very elderly • Octogenarians • Treatment • Guidelines • Management • Mortality

Introduction

Heart failure (HF) is associated with high mortality and prolonged and frequent hospitalizations and is responsible for a tremendous burden on health care systems.¹ The prevalence of this condition increases markedly with age.² Several surveys, including Euro Heart Failure Survey I (EHFS I),³ suggest that outcome is particularly poor in elderly patients⁴ and that treatment is often

complicated by the presence of multiple co-morbid factors.^{4–7} Moreover, evidence-based therapies are less frequently used and underdosage of recommended medications is constantly observed in the elderly.^{8–11} However, EHFS I¹² was performed in 2000–01 at a time when perception of guidelines for the management of HF was less developed than it is nowadays and this survey had a limited follow-up (FU) period of 12 weeks. The purpose of the current study was therefore to (i) analyse the clinical profile and

* Corresponding author. Tel: +33 1 42 16 30 03, Fax: +33 1 42 16 30 20, Email: michel.komajda@pslaphp.fr

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2008. For permissions please email: journals.permissions@oxfordjournals.org.

the outcome of octogenarians enrolled in the Euro Heart Failure Survey II (EHFS II) over a 12 month period, and to (ii) see whether management of HF improved in this more contemporary context when compared with EHFS I.

Methods

EHFS II was conducted by the European Society of Cardiology (ESC) between October 2004 and August 2005 and included 3580 patients admitted to 133 participating hospitals including cardiac care units, intensive care units, as well as on ward facilities (internal medicine and cardiology) in 30 ESC countries.

Methodology and primary results of the survey have been detailed elsewhere.¹³ In brief, EHFS II recruited patients admitted with dyspnoea, and verification of HF based on the presence of symptoms and signs of HF and lung congestion on chest X-ray. Patients were classified by the investigator according to the guidelines on acute HF published by the ESC¹⁴ as follows:

Decompensated HF, acute pulmonary oedema, cardiogenic shock, HF and hypertension, right HF. Clinical history, symptoms, signs, co-morbidities, standard biology, most recent echocardiographic data, and medications at admission and discharge were recorded (for details, see reference 13).

For the conversion of haemoglobin (Hb) and creatinine measurements from SI units, the factors given by Kratz and Lewandrowski¹⁵ were used. Anaemia was defined by the criteria of the World Health Organization¹⁶ (Hb < 13 g/dL in men and < 12 g/dL in women, severe anaemia by Hb < 11.5 g/dL in men and < 10.5 g/dL in women). The glomerular filtration rate (GFR) was calculated according to the abbreviated MDRD formula.¹⁷ Hypertension on admission was defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg. An assessment of preserved left ventricular systolic function was given by echocardiographic left ventricular ejection fraction (EF) > 45%.

This analysis included 3577 patients, 741 (21%) of these patients were ≥ 80 years and we compared their clinical profile, treatment, and mortality with younger patients (*n* = 2836, 79%). In three subjects from the original EHFS II, date of birth was not available and therefore they were not included in the present study. We also examined the proportion of patients treated with high doses of ACE-I (defined as in EHFS I³ by a daily dose of enalapril ≥ 20 mg, captopril ≥ 75 mg, ramipril ≥ 5 mg, perindopril ≥ 4 mg, lisinopril ≥ 20 mg, trandolapril ≥ 2 mg), high doses of ARB (defined by a daily dose of candesartan ≥ 16 mg, eprosartan ≥ 600 mg, irbesartan ≥ 300 mg, losartan ≥ 100 mg, valsartan ≥ 80 mg), and high doses of beta-blockers (defined by a daily dose of bisoprolol ≥ 5 mg, carvedilol ≥ 25 mg, metoprolol succinate ≥ 100 mg, atenolol ≥ 100 mg).

In the centres participating in the FU, 3178 hospital survivors were contacted at 3 months and 12 months post-inclusion. The vital status was ascertained for 2978 patients at median 100 days [inter-quartile range (IQR) 92–116] post-inclusion during the 3 month FU and for 2295 patients at median 372 days (IQR 361–398) in the 1 year FU. Adverse events [death, myocardial infarction (MI), stroke, device implantation, rehospitalization] were recorded if they had occurred since the last contact. For deceased patients, the date of death was collected. The number of hospitalizations since the last contact, but not their exact dates, was collected. At 3 months, 51% of the patients were contacted by phone, 3% by written questionnaire, 27% in person, and for 19%, a hospital record was available. Information at 1 year was obtained by phone for 49%, by written questionnaire for 6%, by patient contact for 24%, and from hospital records for 21%

of the patients. The current medication was recorded for 2464 patients within a period from 70 to 180 days post-inclusion and for 1773 patients between 300 and 540 days.

Statistical analysis

Absolute numbers and percentages are shown for categorical variables to describe the patient population, and medians with IQR for continuous variables. For descriptive purposes, binary variables were compared between subgroups by Pearson's χ^2 test and continuous variables by the Mann–Whitney *U* test. These statistics were calculated for the available cases. Survival after discharge was estimated by the Kaplan–Meier method and compared between age groups by log-rank test. The cumulative incidence of the interval-censored major adverse clinical events (MACE: death, MI, or stroke) since admission was estimated by the product-limit method for the discrete time points discharge, 3 month FU, and 12 month FU. Rehospitalization rates were calculated as the number of rehospitalizations divided by person-months under observation, and rate ratios with 95% confidence intervals were estimated by the Poisson regression with additional dispersion parameter. In the octogenarians, predictors of in-hospital mortality were analysed by multiple logistic regression and predictors of 1 year mortality among the hospital survivors by Cox regression. The following variables were considered as potential predictors on the basis of clinical judgement and a *P*-value < 0.2 in the univariate comparisons: age, gender, body mass index, smoking; clinical classification; diabetes, chronic renal failure, and anaemia; precipitating conditions including acute coronary syndrome, ST-segment elevation myocardial infarction (STEMI), arrhythmias, valvular heart disease, and infection; on admission: somnolence or confusion, cold peripheral temperature, systolic blood pressure, and heart rate; serum creatinine, severe anaemia; EF and health status using the EuroQoL-5D.¹⁸ Prescriptions of ACE-I/ARB, beta-blockers, and statins at discharge were entered into the models of 1 year mortality. The models were finalized regarding the results of stepwise selection procedures using significance levels of 0.1 for entry and 0.15 for removal. Finally, model variables without significant effect are left only for clinical reasons. The discrimination of the logistic regression model was assessed with the *C*-statistic and model calibration with the Hosmer–Lemeshow test. For predictive purposes, the model discrimination and the regression coefficients might be overestimated. In order to assess the predictive accuracy, the models were fitted to 200 bootstrap samples and the estimated coefficients applied to the original data set. Regression in the original sample with the resulting linear predictor as only explanatory variable yields a slope which can be regarded as a factor for shrinkage of the coefficients.¹⁹ The difference between the *C*-statistics evaluated on the bootstrap sample and on the original sample, averaged over the 200 bootstrap replications, is an estimate of optimism, which can be subtracted from the apparent *C*-statistic in order to get a corrected value of the predictive discrimination.²⁰ Octogenarians from EHFS II (overall population and the subgroup with chronic HF and reduced EF) were compared with those from EHFS I, regarding these two surveys as independent cross-sections. The development of drug prescriptions over time was assessed by calculating rates of continuation and discontinuation from admission to discharge, discharge to 3 months, and 3 months to 12 months. The development of the prescription rates was summarized by multiplying the matrices of these transition probabilities in order to avoid apparent changes in prevalence caused by mortality or drop-out. A significance level of 0.05 was assumed for the statistical tests. All *P*-values are results of two-tailed tests. The calculations were performed using SAS[®] statistical software, version 9.1 (Cary, NC, USA).

Results

Patients and demographic characteristics

Out of 3577 patients, there were 741 octogenarians with an age of ≥ 80 years [median age 83.7 years (81.7–86.8)] and 2836 younger patients [median age 68.4 (59.5–74.7)]. Main demographic data on the two age groups (≥ 80 vs. < 80 years) are given in Table 1. Women represented 56% of elderly patients vs. 34% in the younger group, $P < 0.001$. Octogenarians were less commonly referred to a cardiology department than younger subjects (78 vs. 85%, $P < 0.001$). New onset HF (*de novo*) was more frequently observed in older people. Similarly, atrial fibrillation/supraventricular tachycardia and hypertension were also more common in octogenarians. Co-morbidities including stroke/transient ischaemic attack, somnolence/confusion, renal dysfunction, anaemia, and chronic obstructive pulmonary disease (COPD) were more frequent in octogenarians, whereas diabetes was less common.

Table 2 indicates lifestyle characteristics of the overall population. Older people were less likely to live in their own home, had more often walking disorders, self-care problems, and needed more often help by relatives or by assistance services than younger people.

Investigations

Renal function was significantly worse in octogenarians than in younger patients and the prevalence of severe renal dysfunction was increased (Table 3). Similarly, anaemia and severe anaemia were more frequent in older people (Table 1). Echocardiography was less often performed in octogenarians. The proportion of patients with preserved EF ($> 45\%$) was higher in the older group. Overall, octogenarians had a higher EF than younger subjects and a smaller left ventricular end-diastolic diameter. During hospitalization, coronary angiography was less often performed in octogenarians.

Treatment

Comparison of heart failure therapy between octogenarian and younger subjects

Treatment with ACE-I or ARBs, beta-blockers, and spironolactone at the time of discharge from hospital was less commonly prescribed in octogenarians than in younger patients (Figure 1). The combination of ACE-I/ARB + beta-blocker was less frequent in older people (42 vs. 55%, $P < 0.001$), and high doses of ACE-I/ARBs and beta-blockers were less frequently prescribed (high-dose ACE-I/ARB 30 vs. 34.5%, $P < 0.05$; high-dose beta-blockers

Table 1 Baseline clinical characteristics by age group

	Age ≥ 80 years ($n = 741$) (21%)	Age < 80 years ($n = 2836$) (79%)	P-value
Age (years) ^a	83.7 (81.7–86.8)	68.4 (59.5–74.7)	$< 0.001^a$
Male gender	44% (327/741)	66% (1867/2836)	$< 0.001^b$
Body mass index (kg/m^2) ^a	26.0 (23.1–28.9)	26.9 (24.4–30.4)	$< 0.001^a$
Enrolment			
New onset HF (<i>de novo</i>)	45% (333/741)	35% (994/2836)	$< 0.001^b$
HF during past 12 months	37% (267/715)	46% (1278/2753)	$< 0.001^b$
Cardiovascular diseases			
Coronary heart disease	51% (377/741)	54% (1540/2835)	0.094 ^b
Dilated cardiomyopathy	14% (104/735)	21% (583/2823)	$< 0.001^b$
Atrial fibrillation/SVT	48% (351/738)	36% (1028/2829)	$< 0.001^b$
History of hypertension	67% (494/735)	61% (1731/2826)	0.003 ^b
Co-morbidities			
Diabetes	29% (215/739)	34% (955/2832)	0.017 ^b
Stroke or TIA	20% (145/739)	12% (331/2829)	$< 0.001^b$
COPD	22% (164/739)	19% (526/2831)	0.027 ^b
Anaemia (WHO definition) ^c	47% (345/732)	37% (1037/2786)	$< 0.001^b$
Severe anaemia ^d	21% (154/732)	17% (478/2786)	0.015 ^b
Clinical examination			
Systolic blood pressure (mmHg) ^a	140 (120–170)	130 (110–160)	$< 0.001^a$
SBP/DBP $> 140/90$ mmHg	50% (366/737)	41% (1153/2811)	$< 0.001^b$
Somnolence/confusion	24% (171/706)	14% (394/2754)	$< 0.001^b$

Data are presented as percentage (number/population).

HF, heart failure; SVT, supraventricular tachycardia; TIA, transient ischaemic attack; COPD, chronic obstructive pulmonary disease; SBP, systolic blood pressure; DBP, diastolic blood pressure.

^aMedian and quartiles, Mann–Whitney U test.

^bPearson's χ^2 test.

^cHb < 13 g/dL in men, < 12 g/dL in women.

^dHb < 11.5 g/dL in men, < 10.5 g/dL in women.

Table 2 Baseline lifestyle measures by age group

	Age \geq 80 years (n = 741) (21%)	Age < 80 years (n = 2836) (79%)	P-value*
Domestic status			
Living in own home	87% (617/709)	98% (2680/2734)	<0.001
Living alone	21% (144/673)	14% (362/2670)	<0.001
Living with spouse or equal	31% (211/673)	64% (1717/2670)	<0.001
Living in special accommodation	13% (92/709)	2% (54/2734)	<0.001
Need help for services of caring	28% (124/437)	12% (259/2234)	<0.001
Help by relatives in daily activities	41% (186/453)	32% (712/2207)	<0.001
Quality of life			
Self-care problems	59% (270/456)	48% (1081/2261)	<0.001
Walking disorders	80% (364/455)	70% (1586/2261)	<0.001
Difficulties to perform usual activities	79% (357/453)	72% (1626/2257)	0.003
Pain or discomfort	64% (295/458)	66% (1484/2264)	0.641
Anxiety or depression	55% (241/438)	57% (1249/2192)	0.450

Data are presented as percentage (number/population).

*P-values were calculated by Pearson's χ^2 test.

12 vs. 18%, $P < 0.001$). Conversely, diuretic agents and calcium channel blockers (CCB) were more commonly prescribed to octogenarians (diuretics 93 vs. 89.5%, $P < 0.05$; CCB 18 vs. 14%, $P < 0.01$), whereas prescriptions of nitrates and digoxin were similar in both age groups. Anti-arrhythmic agents and lipid-lowering drugs were used less frequently in the older group (13 vs. 19%, $P < 0.001$ and 32 vs. 44%, $P < 0.001$, respectively). In the subgroup of octogenarians with low-EF ($EF \leq 45\%$), the use of ACE-I/ARBs (80 vs. 85%, $P < 0.05$), beta-blockers (60 vs. 69%, $P < 0.01$), combination ACE-I/ARBs + beta-blockers (51 vs. 62.5%, $P < 0.001$), and aldosterone antagonists (48 vs. 58%, $P < 0.01$) remained lower than in younger subjects.

Comparison of heart failure therapy in EHFS II and EHFS I

Table 4 shows a comparison of HF prescriptions between EHFS II and the previous EHFS I in the octogenarians. A significant increase in prescription rates of HF-recommended drugs at discharge was observed in EHFS II. This was shown for ACE-I/ARBs, beta-blockers, and aldosterone antagonists. High doses of ACE-I/ARB/ beta-blockers and the combination of ACE-I/ARBs with beta-blockers were also more frequently used in octogenarians in EHFS II than in EHFS I. Similar findings were observed in the subgroup of octogenarians with chronic HF and reduced EF ($EF \leq 45\%$) (Figure 2).

Prescription rates over time

Figure 3 indicates HF prescription rates over time in the octogenarian group. During 12 months of FU from discharge, the

Table 3 Biological findings and cardiac investigations by age group

	Age \geq 80 years (n = 741) (21%)	Age < 80 years (n = 2836) (79%)	P-value
Laboratory parameters			
Haemoglobin (g/dL) ^a	12.5 (11.2–13.8)	13.2 (11.7–14.5)	<0.001 ^a
Creatinine (mg/dL) ^a	1.3 (1.0–1.7)	1.2 (1.0–1.5)	<0.001 ^a
GFR (MDRD equation) (mL/min) ^a	46.6 (35.5–61.3)	58.7 (43.5–74.7)	<0.001 ^a
GFR < 60 mL/min	73% (523/720)	53% (1459/2768)	<0.001 ^b
GFR < 30 mL/min	16% (118/720)	10% (276/2768)	<0.001 ^b
Echocardiography			
Echocardiography done	81% (598/739)	92% (2613/2833)	<0.001 ^b
Ejection Fraction (%) ^a	40 (30–52)	35 (25–48)	<0.001 ^a
LVEF > 45%	39% (183/470)	28% (624/2260)	<0.001 ^b
LVEDD (mm) ^a	53.4 (47.0–59.0)	59.0 (52.0–66.0)	<0.001 ^a
Left atrial diameter (mm) ^a	46.0 (42.0–51.6)	47.0 (42.0–52.0)	0.177 ^a
Moderate/severe aortic valve stenosis	16% (88/540)	7% (164/2435)	<0.001 ^b
Coronary angiography			
Coronary angiography reported	17% (124/720)	41% (1156/2788)	<0.001 ^b
No significant coronary heart disease	19% (24/124)	32% (368/1156)	0.004 ^b
Percutaneous coronary intervention	5% (35/739)	9% (264/2802)	<0.001 ^b

Data are presented as percentage (number/population).

GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter.

^aMedian and quartiles, Mann–Whitney U test.^bPearson's χ^2 test.

prescription of recommended HF therapies remained stable. Out of the 448 octogenarians whose medication was recorded at 3 months, ACE-I/ARB had been discontinued since discharge in 4.0%, diuretics in 2.7%, beta-blockers in 2.5%, aldosterone antagonists in 2.0%, and digitalis in 3.4%. On the other hand, these drugs had been newly prescribed in 3.6, 2.0, 3.1, 2.7, and 2.9%, respectively. From 3 to 12 months, medication was recorded for 288 octogenarians, the percentages of discontinuation were 5.9, 2.8, 5.2, 5.2, and 4.9%, and the percentages of new prescriptions 2.1, 2.8, 6.3, 5.2, and 3.5%, respectively.

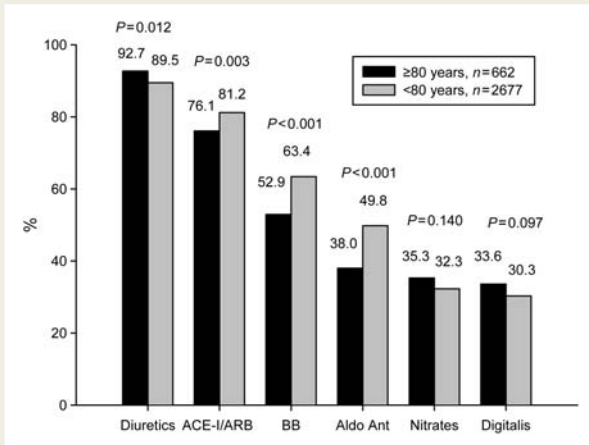


Figure 1 Heart failure medications in Euro Heart Failure Survey II at discharge by age group. ACE-I, angiotensin-converting enzyme-inhibitors; ARBs, angiotensin receptor blockers; BB, beta-blockers; Aldo Ant, aldosterone antagonists. P-values were calculated by Pearson's χ^2 test.

Outcomes

In the overall population, 238 deaths were observed in-hospital, 263 at 3 months, and 319 between 3 and 12 months. During the whole period of observation, overall mortality was higher in the octogenarian group than in the younger group. This applied to in-hospital mortality (10.7 vs. 5.6%, $P < 0.001$), to 3 month mortality after discharge (13.5 vs. 6.8%, $P < 0.001$), as well as 12 month mortality after discharge (28.4 vs. 18.5%, $P < 0.001$) (Figure 4). Similarly, MACE (death, stroke, and acute MI) were more frequent in the older group in hospital (12.9 vs. 9.2%, $P < 0.01$), at 3 months (27.0 vs. 17.7%, $P < 0.001$), and at 12 months after admission (41.7 vs. 29.6%, $P < 0.001$). Finally, rehospitalization rates of survivors were higher in the younger group from discharge to 3 months [0.140 per person-month vs. 0.106 per person-month, rate ratio 1.32 (95% CI 1.11–1.56)] and from 3 to 12 month FU [0.074/month vs. 0.056/month, rate ratio 1.30 (95% CI 1.08–1.57)].

Predictors of death in octogenarians

We examined separately the factors predicting death in hospital and during FU in the octogenarian group. The validation procedures suggested that, for predictive purposes, the effects in the hospital mortality model may be overestimated by ~15% and the adjusted value of the C-statistic would be 0.767; effects in the FU model may be overestimated by 30%. In-hospital mortality was independently associated with age, signs of low cardiac output/cardiogenic shock, STEMI, renal dysfunction, acute infection, and severe disability (confinement to bed) (Table 5). Age remained a strong independent predictor of 1 year mortality in octogenarians surviving at discharge, as well as disability (self-care problems) and co-morbid factors including diabetes and renal dysfunction (Table 6). Prescription of ACE-I/ARBs and statins was associated with a better outcome, whereas the use of beta-

Table 4 Comparison of heart failure medications in discharged alive octogenarians with heart failure in Euro Heart Survey I and II

	EHFS II (n = 662)	EHFS I (n = 2406)	P-value*
Diuretics	93% (612/660)	92% (2209/2398)	0.604
ACE-I	65% (428/660)	53% (1262/2398)	<0.001
ARB	12% (81/661)	4% (93/2398)	<0.001
ACE-I or ARB	76% (503/661)	56% (1344/2398)	<0.001
High-dose ACE-I	26% (167/653)	16% (372/2311)	<0.001
High-dose ARB	5% (33/659)	0.5% (13/2395)	<0.001
High-dose ACE-I or ARB	30% (199/661)	16% (385/2398)	<0.001
Beta-blockers	53% (349/660)	25% (593/2398)	<0.001
High-dose beta-blockers	12% (79/659)	5% (123/2354)	<0.001
ACE-I or ARB and beta-blockers	42% (279/661)	15% (348/2398)	<0.001
Spironolactone/epplerone	38% (251/660)	15% (355/2398)	<0.001
Digitalis	34% (222/660)	38% (919/2398)	0.027
Calcium channel blockers	18% (122/660)	21% (501/2398)	0.174

Data are presented as percentage (number/population).

ACE-I, angiotensin-converting enzyme-inhibitors; ARB, angiotensin receptor blockers.

*P-values were calculated by Pearson's χ^2 test.

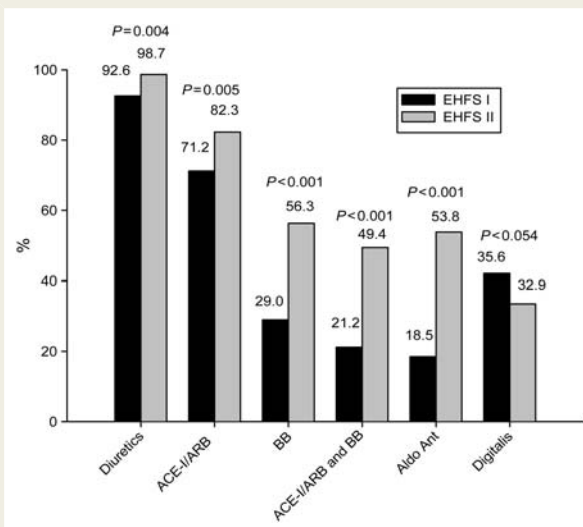


Figure 2 Comparison of heart failure medications at discharge in octogenarians in Euro Heart Failure Survey I ($n = 542$) and II ($n = 158$), $EF < 45\%$. ACE-I, angiotensin-converting enzyme-inhibitors; ARBs, angiotensin receptor blockers; BB, beta-blockers; Aldo Ant, aldosterone antagonists. P -values were calculated by Pearson's χ^2 test.

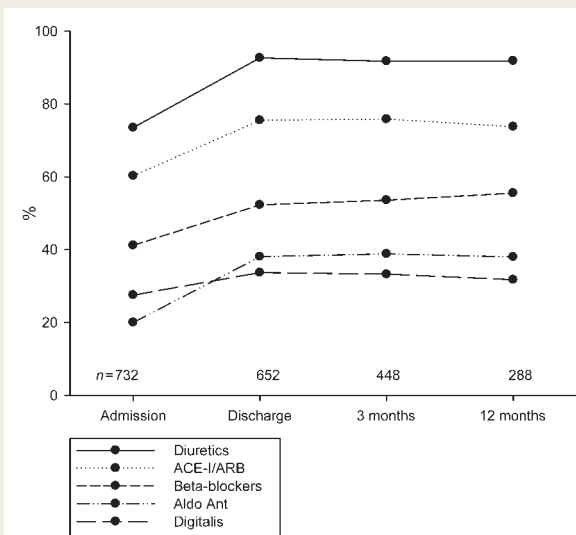


Figure 3 Heart failure prescription rates over time in the octogenarian group. ACE-I, angiotensin-converting enzyme-inhibitors; ARBs, angiotensin receptor blockers; Aldo Ant, aldosterone antagonists.

blockers at discharge was predictive of good outcome only in the subgroup with reduced EF ($EF \leq 45\%$) [HR 0.56 (95% CI: 0.33–0.94), $P < 0.05$]. EF as a continuous variable was not predictive of in-hospital or follow up-mortality of the octogenarian population in the multivariate model and was predictive of in-hospital death only in the subgroup with reduced EF [OR 1.32 (95% CI 1.01–1.72) per 5% decrease].

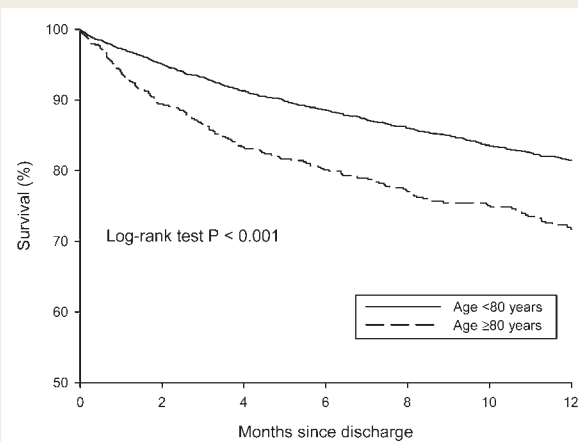


Figure 4 Overall mortality after discharge according to age.

Table 5 Predictors of hospital mortality in octogenarians

Variable	Bivariate odds ratio (95% CI) ^a	Adjusted odds ratio (95% CI) ^b
Age (per 5 year increase)	1.36 (1.01–1.82)	1.42 (1.04–1.95)
Cardiogenic shock	12.99 (5.28–31.97)	5.20 (1.77–15.33)
STEMI	3.02 (1.65–5.53)	3.62 (1.79–7.32)
SBP (per 10 mmHg decrease)	1.19 (1.10–1.29)	1.09 (1.01–1.18)
Confinement to bed	4.31 (2.09–8.89)	3.08 (1.32–7.20)
Acute infection	1.79 (1.04–3.07)	1.96 (1.08–3.58)
Somnolence/confusion	3.48 (2.13–5.66)	1.97 (1.10–3.55)
Cold periphery	3.17 (1.79–5.60)	1.92 (1.00–3.69)
Creatinine (mg/dL)	1.69 (1.28–2.24)	1.63 (1.17–2.27)

$C = 0.793$, Hosmer–Lemeshow test $P = 0.60$.

STEMI, ST-segment elevation myocardial infarction; SBP, systolic blood pressure.

^aCalculated by simple logistic regression separately for each variable.

^bCalculated by multiple logistic regression, including all the factors shown in the table as co-variables.

Discussion

Clinical profile

We observed clinical differences between octogenarians and younger patients consistent with previous studies.^{3,4,7,9–11} Older subjects were more frequently women, had lower BMI, and higher blood pressure levels. As observed previously in EHFS-I,³ the presence of co-morbidities (stroke, COPD, anaemia, renal dysfunction, and neurological disorders) was also more common in octogenarians,^{3,4,7,9} and the frequency of diabetes was lower in older patients. This may be related to the high mortality rate in patients with diabetes, reducing therefore the likelihood of survival until the age of 80 years. Atrial fibrillation was more often observed in the octogenarians^{4,9–11} and was

Table 6 Predictors of follow-up mortality after discharge in octogenarians

Variable	Crude hazard ratio (95% CI) ^a	Adjusted hazard ratio (95% CI) ^b
Age (per 5 year increase)	1.55 (1.29–1.87)	1.51 (1.24–1.84)
SBP (per 10 mmHg decrease)	1.05 (1.00–1.10)	1.04 (0.99–1.09)
Diabetes mellitus	1.36 (0.98–1.89)	1.56 (1.12–2.18)
Self-care problems	1.82 (1.21–2.75)	1.60 (1.03–2.49)
Creatinine (mg/dL)	1.51 (1.26–1.80)	1.48 (1.21–1.80)
ACE-inhibitors/ARB	0.48 (0.35–0.66)	0.56 (0.40–0.79)
Statins	0.59 (0.41–0.85)	0.67 (0.45–0.99)
Beta-blockers	0.72 (0.53–0.98)	0.87 (0.63–1.20)

SBP, systolic blood pressure; ARB, angiotensin receptor blockers.
^aCalculated by simple Cox regression separately for each variable.
^bCalculated by multiple Cox regression, including all the factors shown in the table as co-variables.

present in half of the patients as in EHFS I.³ Interestingly, new onset HF (*de novo*) was more frequently reported in the octogenarian group. To our knowledge, this has not been investigated in other studies. The reasons for the increased rate of *de novo* HF episode in the octogenarians might be related to the high frequency of preserved EF after 80 years.

Lifestyle

Our findings indicate a high rate of dependency and a low quality of life in elderly HF people. These results suggest a stronger decline in functional status in octogenarians with HF compared with those without HF.^{21,22} This increased disability was associated to a higher need for household assistance services in older persons. Overall, our results suggest that the elderly HF patients are very frail patients. Thus, there is room for improving daily care by multi-disciplinary approaches in these patients.

Investigations

We observed a marked improvement in the rate of performance of echocardiography in octogenarians people compared with previous studies. In octogenarian patients, cardiac function was assessed twice more often in EHF II than in EHFS I.³ These results can be explained by an improvement in health care quality over the past years or by the fact that more patients enrolled in EHFS II were referred to cardiology departments than in EHFS I.

Nevertheless, assessment of cardiac function remained less common in older patients. Left ventricular EF was more frequently preserved in the older subjects as reported in other studies.^{23,24} Finally, coronary angiography was twice less often performed in octogenarians than in younger subjects.²⁵ This observation may be partly explained by the high rate of renal dysfunction and of co-morbidities in the older group.

Treatment

As observed previously, there was an underprescription of recommended HF medications, in the octogenarian patients enrolled in EHFS II.^{3,4,7,9,26} The difference was mainly observed for beta-blockers and aldosterone antagonists, which are less often used in octogenarians. A number of factors related to patients (general condition, co-morbidities, poor tolerance) or to prescribers (lack of awareness of evidence-based guidelines, fear of side effects, focus on symptomatic improvement rather than on outcome) have been suggested to explain this situation.²⁷

However, a striking finding of our survey was the substantial increase in the rate of prescription of recommended medications at discharge when compared with the first European Survey.³ This was observed in the overall HF population as well as in the subgroup with reduced EF. In this subset, the rate of prescription of ACE-I/ARBs was >80%, beta-blocker use was nearly doubled when compared with EHFS I, and half of the population received the combination. Finally, we observed a much higher rate of prescription of aldosterone antagonists than previously reported in EHFS I. Caution has been recommended in the use of this class in the very elderly because of the risk of potentially severe side effects in relation to the high prevalence of renal dysfunction.²⁸ It is likely that the inclusion criteria of the current survey, namely the context of acute/decompensated HF, played a role to explain this finding.

There was also an increase in the rate of prescription of recommended medications from admission to discharge, and, most importantly, the improvement in the rate of prescription was sustained over the 12 month FU period in survivors. Particularly, very little changes in drug therapy occur after hospital discharge. These results have been obtained also in other studies²⁹ and emphasize the major role of the early treatment initiation for the long-term HF therapy in the elderly. Overall, our results suggest an improvement in treatment modalities in the very elderly with HF. This might reflect the impact of the large dissemination of international guidelines and a better knowledge of the objectives of the treatment, particularly among cardiologists.³⁰

Outcomes

Few studies have so far followed up cohorts of elderly patients over 80 years for 1 year after index hospitalization. In-hospital, 3 month and 12 month mortality rates were extremely high in the octogenarian population. The rate of major cardiovascular events observed during the FU period was also significantly increased. Our results also confirm that age appears as a strong and independent predictor of mortality in HF patients.^{31,32}

Factors associated with mortality in hospital and during FU were different. In-hospital death was mainly related to acute clinical conditions, whereas long-term mortality was associated with disability³³ and the presence of co-morbidities such as diabetes and renal dysfunction. As reported previously, we showed that renal function is a strong predictor of both in-hospital and FU mortality,³⁴ whereas anaemia was not associated with poor outcome in octogenarians (as observed in EHFS I³). Low EF, a strong predictor of mortality in younger population,³⁵ was not identified here as an independent factor in the octogenarian population, unlike the

report from a recent national survey.⁴ This finding may be due to the high prevalence of HF with preserved EF, and, indeed, only one-fifth of the available echo results showed an EF < 30%. The use of ACE-I or ARBs was associated with a better 1 year outcome.^{36–39} This finding is consistent with the previous EHFS I and suggests that ACE-I/ARBs should be used over 80 years in HF patients. The fact that prescription of beta-blockers was not associated to improvement in 1 year mortality in the overall population could be related to the high proportion of HF with preserved EF or to the fact that the limited size of the population taking this medication did not allow to show benefit.

Surprisingly, we observed a higher rehospitalization rate in younger people. This might be due to the fact that octogenarians had a higher mortality during hospitalization. So the more severe patients were likely to die early, resulting in a competing risk.

Limitations

Our survey was an observational study conducted only in patients hospitalized with HF. Sites that volunteered for the study included a majority of cardiology departments. Therefore, the proportion of octogenarians referred to internal medicine wards was lower in the second survey when compared with the first one. This fact may partly explain the improvement in HF management observed here. It has been demonstrated in other studies that patients treated by cardiologists are more likely to receive HF-recommended drugs on admission and at discharge compared with patients treated by other physicians.³⁰ Our results are in line with these findings and suggest that cardiologists are more aware of and better apply the guidelines for HF therapy in the elderly. Moreover, the observed differences in HF prescriptions between the two surveys were not related to different frequencies of co-morbidities. Indeed, at discharge, the prevalence of renal dysfunction, COPD, stroke, and anaemia was similar in EHFS I and EHFS II.

In our study, high disability was observed in HF octogenarians on the basis of self-related questionnaire but we did not record all co-morbid factors associated with ageing, and this might have resulted in an underestimate of the overall prevalence. Particularly, presence of dementia or cancer was not evaluated and could not be included in the predictive model of mortality. Moreover, no central laboratory was used for echocardiography assessment. Therefore, caution is needed in the interpretation of cardiac function.

The effect of treatments on outcome must be cautiously interpreted in the context of an observational study which was not designed to evaluate the impact of prescriptions on prognosis. Furthermore, the inclusion criteria used in EHFS II were partly different from those used in EHFS I, and patients were not exactly superimposable, but the clinical profile of the octogenarians was similar in the two surveys, particularly in terms of co-morbidities. Moreover, the diagnostic criteria used in the current survey were more robust than those of EHFS I, where patients with suspected or confirmed HF were included. Finally, the comparison of treatment modalities in the octogenarians in the two surveys showed an improvement not only in the overall population but also and more specially in the low-EF subgroup of patients, a domain where international guidelines are well established.

Conclusions

We report here a large cohort of octogenarian people with acute/decompensated HF. Compared with younger patients, octogenarians had more co-morbidities and a higher mortality rate over 12 months of FU. Diagnostic procedures and medical management remain suboptimal but are improving when compared with the previous European survey.

Conflict of interest: none declared.

References

1. Redfield MM. Heart failure—an epidemic of uncertain proportions. *N Engl J Med* 2002;**347**:1442–1444.
2. McMurray JJ, Pfeffer MA. Heart failure. *Lancet* 2005;**365**:1877–1889.
3. Komajda M, Hanon O, Hochadel M, Follath F, Swedberg K, Gitt A, Cleland JG. Management of octogenarians hospitalized for heart failure in Euro Heart Failure Survey I. *Eur Heart J* 2007;**28**:1310–1318.
4. Mahjoub H, Rusinaru D, Soulière V, Durier C, Peltier M, Tribouilloy C. Long-term survival in patients older than 80 years hospitalised for heart failure. A 5-year prospective study. *Eur J Heart Fail* 2008;**10**:78–84.
5. Gambassi G, Forman DE, Lapane KL, Mor V, Sgadari A, Lipsitz LA, Bernabei R. Management of heart failure among very old persons living in long-term care: has the voice of trials spread? The SAGE Study Group. *Am Heart J* 2000;**139**:85–93.
6. Lien CT, Gillespie ND, Struthers AD, McMurdo ME. Heart failure in frail elderly patients: diagnostic difficulties, co-morbidities, polypharmacy and treatment dilemmas. *Eur J Heart Fail* 2002;**4**:91–98.
7. Havranek EP, Masoudi FA, Westfall KA, Wolfe P, Ordian DL, Krumholz HM. Spectrum of heart failure in older patients: results from the National Heart Failure project. *Am Heart J* 2002;**143**:412–417.
8. Heart failure treatment with angiotensin-converting enzyme inhibitors in hospitalized Medicare patients in 10 large states. The Large State Peer Review Organization Consortium. *Arch Intern Med* 1997;**157**:1103–1108.
9. Gustafsson F, Torp-Pedersen C, Seibaek M, Burchardt H, Kober L, DIAMOND study group. Effect of age on short and long-term mortality in patients admitted to hospital with congestive heart failure. *Eur Heart J* 2004;**25**:1711–1717.
10. Pulignano G, Del Sindaco D, Tavazzi L, Lucci D, Gorini M, Leggio F, Porcu M, Scherillo M, Opasich C, Di Lenarda A, Senni M, Maggioni AP, IN-CHF Investigators. Clinical features and outcomes of elderly outpatients with heart failure followed up in hospital cardiology units: data from a large nationwide cardiology database (IN-CHF Registry). *Am Heart J* 2002;**143**:45–55.
11. Cohen-Solal A, Desnos M, Delahaye F, Emeriau JP, Hanania G. A national survey of heart failure in French hospitals. The Myocardiopathy and Heart Failure Working Group of the French Society of Cardiology, the National College of General Hospital Cardiologists and the French Geriatrics Society. *Eur Heart J* 2000;**21**:763–769.
12. Cleland JG, Swedberg K, Follath F, Komajda M, Cohen-Solal A, Aguilar JC, Dietz R, Gavazzi A, Hobbs R, Korewicki J, Madeira HC, Moiseyev VS, Preda I, van Gilst WH, Widimsky J, Freemantle N, Eastaugh J, Mason J. Study Group on Diagnosis of the Working Group on Heart Failure of the European Society of Cardiology. The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003;**24**:442–463.
13. Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola VP, Hochadel M, Komajda M, Lassus J, Lopez-Sendon JL, Ponikowski P, Tavazzi L; EuroHeart Survey Investigators; Heart Failure Association, European Society of Cardiology. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. *Eur Heart J* 2006;**27**:2725–2736.
14. Nieminen MS, Böhm M, Cowie MR, Drexler H, Filippatos GS, Jondeau G, Hasin Y, Lopez-Sendon J, Mebazaa A, Metra M, Rhodes A, Swedberg K, Priori SG, Garcia MA, Blanc JJ, Budaj A, Cowie MR, Dean V, Deckers J, Burgos EF, Lekakis J, Lindahl B, Mazzotta G, Morais J, Oto A, Smiseth OA, Garcia MA, Dickstein K, Albuquerque A, Conthe P, Crespo-Leiro M, Ferrari R, Follath F, Gavazzi A, Janssens U, Komajda M, Morais J, Moreno R, Singer M, Singh S, Tendera M, Thygesen K, ESC Committee for Practice Guideline (CPG) Executive summary of the guidelines on the diagnosis and treatment of acute heart failure: the task force on acute heart failure of the European Society of Cardiology. *Eur Heart J* 2005;**26**:384–416.
15. Kratz A, Lewandowski KB. Normal Reference Laboratory Values. *N Engl J Med* 1998;**339**:1063–1071.

16. Izaks GJ, Westendorp RG, Knook DL. The definition of anemia in older persons. *JAMA* 1999;**12**:1714–1717.
17. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G, National Kidney Foundation. National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: evaluation, classification, and stratification. *Ann Intern Med* 2003;**139**:137–147.
18. Brooks R, Rabin R, de Charro F. The measurement and valuation of health status using EQ-5D: a European perspective. *Dordrecht* 2003;1–19.
19. Steyerberg EW, Eijkemans MJC, Harrell FE Jr, Habbema JDF. Prognostic modelling with logistic regression analysis: a comparison of selection and estimation methods in small data sets. *Stat Med* 2000;**19**:1059–1079.
20. Harrell FE, Lee KL, Mark DB. Tutorial in biostatistics. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med* 1996;**15**:361–387.
21. Hoeymans N, Feskens EJ, van den Bos GA, Kromhout D. Age, time, and cohort effects on functional status and self-rated health in elderly men. *Am J Public Health* 1997;**87**:1620–1625.
22. Beckett LA, Brock DB, Lemke JH, Mendes de Leon CF, Guralnik JM, Fillenbaum GG, Branch LG, Wetle TT, Evans DA. Analysis of change in self-reported physical function among older persons in four population studies. *Am J Epidemiol* 1996;**143**:766–778.
23. Hogg K, Swedberg K, McMurray J. Heart failure with preserved left ventricular systolic function; epidemiology, clinical characteristics, and prognosis. *J Am Coll Cardiol* 2004;**43**:317–327.
24. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med* 2006;**355**:251–259.
25. Mehta RH, Rathore SS, Radford MJ, Wang Y, Wang Y, Krumholz HM. Acute myocardial infarction in the elderly: differences by age. *J Am Coll Cardiol* 2001;**38**:736–741.
26. Forman DE, Chander RB, Lapane KL, Shah P, Stoukides J. Evaluating the use of angiotensin-converting enzyme inhibitors for older nursing home residents with chronic heart failure. *J Am Geriatr Soc* 1998;**46**:1550–1554.
27. Ahmed A, Weaver MT, Allman RM, DeLong JF, Aronow WS. Quality of care of nursing home residents hospitalized with heart failure. *J Am Geriatr Soc* 2002;**50**:1831–1836.
28. Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. *N Engl J Med* 2004;**351**:543–551.
29. Gislason GH, Rasmussen JN, Abildstrom SZ, Schramm TK, Hansen ML, Buch P, Sørensen R, Folke F, Gadsbøll N, Rasmussen S, Køber L, Madsen M, Torp-Pedersen C. Persistent use of evidence-based pharmacotherapy in heart failure is associated with improved outcomes. *Circulation* 2007;**116**:737–744.
30. Foody JM, Rathore SS, Wang Y, Herrin J, Masoudi FA, Havranek EP, Krumholz HM. Physician specialty and mortality among elderly patients hospitalized with heart failure. *Am J Med* 2005;**118**:1120–1125.
31. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. *JAMA* 2003;**290**:2581–2587.
32. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB, Ostergren J, Michelson EL, Pieper KS, Granger CB. Predictors of mortality and morbidity in patients with chronic heart failure. *Eur Heart J* 2006;**27**:65–75.
33. Cacciatore F, Abete P, Mazzella F, Viati L, Della Morte D, D'Ambrosio D, Gargiulo G, Testa G, Santis D, Galizia G, Ferrara N, Rengo F. Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *Eur J Clin Invest* 2005;**35**:723–730.
34. Smith GL, Lichtman JH, Bracken MB, Shlipak MG, Phillips CO, DiCapua P, Krumholz HM. Renal impairment and outcomes in heart failure: systematic review and meta-analysis. *J Am Coll Cardiol* 2006;**47**:1987–1996.
35. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. *J Am Coll Cardiol* 1999;**33**:1948–1955.
36. Masoudi FA, Rathore SS, Wang Y, Havranek EP, Curtis JP, Foody JM, Krumholz HM. National patterns of use and effectiveness of angiotensin-converting enzyme inhibitors in older patients with heart failure and left ventricular systolic dysfunction. *Circulation* 2004;**110**:724–731.
37. Gianni M, Bosch J, Pogue J, Probstfield J, Dagenais G, Yusuf S, Lonn E. Effect of long-term ACE-inhibitor therapy in elderly vascular disease patients. *Eur Heart J* 2007;**28**:1382–1388.
38. Havranek EP, Abrams F, Stevens E, Parker K. Determinants of mortality in elderly patients with heart failure: the role of angiotensin-converting enzyme inhibitors. *Arch Int Med* 1998;**158**:2024–2028.
39. Johnson D, Jin Y, Quan H, Cujec B. Beta-blockers and angiotensin-converting enzyme inhibitors/receptors blockers prescriptions after hospital discharge for heart failure are associated with decreased mortality in Alberta, Canada. *J Am Coll Cardiol* 2003;**42**:1438–1445.